REMARKS

Claims 1-32 are pending in this application. Claims 1-32 are rejected under 35 U.S.C. § 103(a) for obviousness over Lee et al. (U.S. Patent No. 6,117,456; hereinafter "the '456 patent"). Claims 1-8, 11, 12, 13, 14-19, and 22-32 are rejected for obviousness-type double patenting over claims 4, 5, 7, 8, and 14 of U.S. Patent No. 6,587,341, and claims 9, 10, 20, and 21 are rejected for obviousness-type double patenting over claims 4, 5, 7, 8, and 14 of U.S. Patent No. 6,287,341 in view of the '456 patent. By this reply, Applicants cancel claims 14 and 15, add new claims 33-36, and address each of the Examiner's rejections below.

Support for the Amendment

Support for new claims 33-36 is found in the specification, e.g., at page 14, lines 10-19. No new matter is added by the amendment.

Rejections under 35 U.S.C. § 103(a)

Claims 1-32 are rejected under 35 U.S.C. § 103(a) for obviousness over the '456 patent. The Examiner states that the '456 patent discloses:

> a material for in vivo applications that can be formed or "machined" into an implant including...[a first and second calcium phosphate, and that] a supplementary material may be added to the precursors to improve the hardness or compressive strength of the poorly crystalline hydroxyapatite. Although...[the '456 patent does] not disclose specific compressive strengths of 60 MPa or 120 MPa, it would have been obvious to one having ordinary skill in the art at the time the invention was made to have adjusted the hardness or compressive strength of the poorly crystalline hydroxyapatite, since it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. *In re Aller*, 105 USPQ 233.

Applicants respectfully traverse this rejection.

The M.P.E.P. § 2143 states:

> To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations.

The '456 patent discloses a self-hardening bioceramic composition that is, for a period of time, workable at room temperature, readily formable and/or injectable. The composition includes a hydrated precursor of a calcium phosphate and an aqueous-based liquid in an amount sufficient to hydrate the calcium phosphate to form a paste or putty. The paste or putty hardens in an endothermic reaction to form a poorly crystalline apatitic calcium phosphate. (See col. 4, lines 3-46).

The '456 patent states that supplementary material, e.g., sponges, meshes, films, fibers, gels, and filaments or particles, may be selected to improve tensile strength and hardness of the bioceramic composition (see col. 22, lines 30-31). The '456 patent does not teach or suggest that the addition of any of these materials will necessarily produce a bioceramic composition with a hardness of at least about 60 MPa, or even that such a hardness could be achieved by addition of one or more of these materials. The '456 patent provides only one example, Example 13, that demonstrates that the hardness of the bioceramic composition is 7-9 MPa (see Example 13, col. 30, lines 44-57).

Applicants' independent claims 1, 16, 25, 28, and 31-32, and their dependent claims 2-13, 17-24, 26-27, and 29-30, are directed to calcium phosphate bone implants having a compressive strength of at least about 60 MPa, and methods of bone implantation and spinal fusion that employ such implants. The specification states that "[h]ydroxyapatite solids...have been reported that are resorbable, but [these solids] are not strong enough for spinal fusion applications or other applications requiring high strength materials" (see page 2, lines 16-18, of the present application). The specification further teaches that in spinal fusion applications:

> The high strength of the bone substitute material implants of the invention helps to immobilize the vertebrae until remodeling is complete. Remodeling of the bone substitute material implants of the invention is a long-term process, occurring on a time scale of months to years. For example, a bone substitute material dowel of the invention may be converted fully into bone in about two years. Remodeling proceeds slowly due to the high density of the bone substitute material implants of the invention. (See page 13, lines 4-9.)

The '456 Patent Does Not Teach or Suggest Every Limitation of the Present Claims

As is discussed above, the '456 patent does not disclose or suggest Applicants' claimed implants having a compressive strength of at least about 60 MPa. The '456 patent teaches a hydrated precursor calcium phosphate material in the form of a malleable paste or putty, which hardens to form a solid poorly crystalline apatitic calcium phosphate material. A malleable paste or putty as taught by the '456 patent would not be expected to provided any great degree of compressive strength, and even the disclosed hardened poorly crystalline apatitic calcium phosphate material would not be expected to afford the high compressive strength of at least about 60 MPa, as is recited in Applicants' claims. Indeed, as is discussed above, the only specific example of implant compressive strength provided in the '456 patent is Example 13,

which discloses a compressive strength of 7-9 MPa for a hardened poorly crystalline apatitic calcium phosphate material manufactured according to the methods of the '456 patent (see column 30, lines 56-57). A compressive strength of 7-9 MPa is substantially lower, by an order of magnitude, than the high compressive strength of at least about 60 MPa recited in Applicants' claims.

The Examiner recognizes that the '456 patent does not disclose a compressive strength of at least about 60 MPa, as is recited in independent claims 1, 16, 25, 28, and 31-32, and claims dependent therefrom, but asserts that it would have been obvious to one of ordinary skill in the art to adjust the hardness or compressive strength of the poorly crystalline hydroxyapatite, because where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. Applicants did not merely use ordinary skill to identify optimum or workable ranges, but instead exercised inventive skill to develop a material that provides a particular desired property, namely, a high compressive strength of about 60 MPa or greater. Applicants' specification discloses inventive bone implants that have a compressive strength of at least about 60 MPa both in dry precursor form and upon hydration at body temperature (see the specification, e.g., at page 18, lines 7-15). As is described in Applicants' specification, prior to Applicants' invention, despite the existence of various known bone implant materials, a ceramic implant that is biocompatible and resorbable, yet strong enough for use in high strength applications remained elusive (page 2, line 22 – page 3, line 3). That is, while one of ordinary skill in the art might have desired to improve implant strength for certain applications, actually providing a high strength biocompatible, resorbable implant was not merely a matter of adjusting known parameters.

In further support of Applicants' position that the '456 patent fails to teach or suggest all of the limitations of the present claims (i.e., a bone implant with a compressive strength of at least about 60 MPa), Applicants provide herewith the Declaration of Dr. Aliassghar N. Tofighi. The Tofighi Declaration states that the methods of the '456 patent would not have produced a bioceramic composition with a compressive strength of at least about 60 MPa, either with or without the addition of any of the supplementary materials described in the '456 patent specification (see paragraph 5 of the Tofighi Declaration). Dr. Tofighi, who is also a listed inventor of the '456 patent, states that manufacture of the presently claimed bone implant having a compressive strength of at least about 60 MPa could not have been achieved using only the guidance of the '456 patent and routine skill in the art, as is suggested by the Examiner, because the '456 patent does not teach or suggest the high energy grinding step taught in the present specification (see, e.g., Example 3, page 21, line 7, through page 22, line 1), which yields an intimately mixed calcium phosphate powder, which is required to produce the presently claimed bone implant (see paragraph 5 of the Tofighi Declaration). Therefore, the presently claimed bone implant having a compressive strength of at least about 60 MPa and methods of its production are not obvious in view of the '456 patent.

The '456 Patent Does Not Provide Any Reasonable Expectation of Success

The '456 patent also does not include any specific teachings that disclose, suggest, or provide one of ordinary skill in the art with a reasonable expectation of success in making and using high compressive strength implants, as is recited in Applicants' claims. For example, as is discussed above, hardness testing of a PCA calcium phosphate prepared according to the method

of the '456 patent confirms that the PCA calcium phosphate has a compressive strength of about 7-9 MPa (see col. 30, lines 44-57, of the '456 patent), which is an order of magnitude less than the 60 MPa compressive strength of the presently claimed bone implant. One skilled in the art, upon reading the '456 patent, would have no reasonable expectation that a bone implant prepared according to the method of the '456 patent would have a compressive strength of at least about 60 MPa. Further, the '456 patent lacks any enabling disclosure of how one skilled in the art could or should modify the method of the '456 patent to yield a bone implant with a compressive strength of at least about 60 MPa. Absent any teaching or suggestion that the methods of the '456 patent would produce a bone implant with a compressive strength 10 times greater than the 7-9 MPa disclosed in Example 13, the '456 patent does not provide any reasonable expectation of success in making a bone implant having the characteristics recited in the present claims. Therefore, the '456 patent cannot be used to support a *prima facie* case of obviousness against pending claims 1-36 (see M.P.E.P. § 2143).

Other Features that Distinguish the Present Claims from the '456 Patent

While the foregoing arguments distinguish all of the pending claims 1-13 and 16-32 over the disclosure of the '456 patent, additional distinctions apply with respect to some of Applicants' claims. For example, claims 3-4, 16, 28, and 32 recite a first calcium phosphate in intimate mixture with a second calcium phosphate. "Intimate mixture" is defined in the specification (page 7, line 22 – page 8, line 1) to mean that particles of the two calcium phosphate materials are intermixed on a nanometer scale. This intimate mixture allows for efficient reaction of the two calcium phosphate materials to form poorly-crystalline

hydroxyapatite upon implantation *in vivo* (page 8, lines 6-8). The '456 patent does not disclose such an intimate mixture of two calcium phosphate materials, but rather focuses on mixing two calcium phosphates together with an aqueous-based liquid to form a paste or putty that hardens into poorly crystalline hydroxyapatite. Accordingly, the '456 patent does not render obvious Applicants' claims 3-4, 16, 28, and 32, which recite two calcium phosphate materials in intimate mixture, or the associated dependent claims 5-8, 17-24, and 29-30.

Claims 10, 12-13, 21, and 23-24 recite an implant having a compressive strength of at least about 120 MPa. As is discussed above, the '456 patent does not teach or suggest a method for manufacturing a bone implant having a compressive strength of at least about 60 MPa. For this reason as well, the '456 patent does not teach or suggest or provide a reasonable expectation of success in achieving a bone implant having this even higher degree of compressive strength. Thus, claims 10, 12-13, 21, and 23-24 are not obvious over the '456 patent.

Claims 26 and 29 recite methods of bone implantation in which conversion of the implanted calcium phosphate material to poorly-crystalline hydroxyapatite is completed in a time between about 2 weeks and about 6 weeks after implantation. The Examiner recognized that the '456 patent does not disclose such conversion times, but argued that it would have been obvious in view of the '456 patent to select materials to produce a conversion time within the claimed range of about 2 weeks to about 6 weeks. On the contrary, the '456 patent teaches that the disclosed self-hardening composition hardens to form poorly crystalline apatitic calcium phosphate much more quickly *in vivo*, generally within a period of under five *hours* (column 11, lines 29-33; column 16, lines 53-55; column 18, lines 44-50). The '456 patent does not teach or suggest, or give any motivation to provide, a bone implant material that instead converts to

poorly-crystalline hydroxyapatite over a period of *weeks* after implantation, as is recited in present claims 26 and 29. Rather, the '456 patent teaches away from the claimed slowly converting material by disclosing much shorter *in vivo* conversion times. Thus, the slowly converting material recited in claims 26 and 29 is not rendered obvious by the '456 patent (see, e.g., M.P.E.P. § 2144.05(B)(III)).

For the reasons described above, the '456 patent does not teach or suggest Applicants' claimed high strength calcium phosphate implants and related methods, or provide a reasonable expectation of success in achieving these particular materials or methods. Thus, *prima facie* obviousness has not been established, and the pending claims 1-13 and 16-32 are not obvious over the '456 patent. The same analysis would apply with respect to new dependent claims 33-36, which depend from rejected claims 1, 16, 25, and 28, respectively, to the extent that the Examiner would apply the obviousness rejection to the new claims. The obviousness rejection is moot with respect to claims 14-15, which have been canceled. Accordingly, Applicants respectfully request that the present rejection under 35 U.S.C. § 103(a) be reconsidered and withdrawn.

Rejection of Claims 1-32 for Obviousness-Type Double Patenting

Claims 1-8, 11-19, and 22-32 are rejected for obviousness-type double patenting over claims 4-5, 7-8, and 14 of U.S. Patent No. 6,287,341 ("the '341 patent"). Claims 9-10 and 20-21 are rejected for obviousness-type double patenting over claims 4-5, 7-8, and 14 of the '341 patent in view of the '456 patent.

As is described above, Applicants' pending claims 1-13 and 16-32 are directed to calcium phosphate bone implants having a compressive strength of at least about 60 MPa, and methods of bone implantation and spinal fusion employing such implants.

Claims 4-5, 7-8, and 14 of the '341 patent are directed to a calcium phosphate implant material in the form of a paste or putty, and methods of preparing such a material.

To support an obviousness-type double patenting rejection, a claim in the application must define an invention that is merely an obvious variation of an invention claimed in the cited patent. The focus of any double-patenting analysis is on the claims involved. In determining whether an invention defined in a claim of an application is an obvious variation of the invention defined in the claim of a patent, the disclosure of the patent may not be used as prior art. MPEP § 804.

The cited claims of the '341 patent recite a paste or putty implant material. The claims do not address the compressive strength of the paste or putty. A paste or putty is generally understood to be a soft, malleable material that would not provide a compressive strength of at least about 60 MPa, as is recited in Applicants' claims 1-13 and 16-32. The Examiner argued that the '341 patent discloses formulating an implant to improve strength for load-bearing applications, and that the claimed compressive strengths would have been an obvious design choice. For purposes of the present double patenting analysis, Applicants' claims should be evaluated only with respect to the cited *claims* of the '341 patent, and the disclosure of the patent may not be used as prior art. Because the cited claims of the '341 patent recite a paste or putty (i.e., a formable material that would not be expected to provide a compressive strength of at least

60 MPa) and make no reference to compressive strength, Applicants' pending claims 1-13 and 16-32 are patentably distinct from the cited claims.

Further distinction of Applicants' pending claims over the cited claims of the '341 patent can be made. For example, Applicants' claim 2 recites an implant that is a machined article. Such a machined article is patentably distinct from a soft paste or putty material as recited in the cited claims 4-5, 7-8, and 14 of the '341 patent. The Examiner asserted that the '341 patent discloses shaping an implant using drills and other known shaping tools. As is described above, such reference to the specification of the '341 patent is improper for the purposes of a double patenting analysis when the cited claims provide no basis for such reference. Because the cited claims recite a paste or putty material and make no mention of machining the material, the machined article recited in Applicants' claim 2 is patentably distinct from the claims of the '341 patent.

Applicants' claims 3-4, 16, 28, and 32 recite a first calcium phosphate in intimate mixture with a second calcium phosphate. As is discussed above, "intimate mixture" is defined in the specification to mean that particles of the two calcium phosphate materials are intermixed on a nanometer scale. Nothing in the cited claims discloses or suggests such an intimate mixture. Thus, Applicants' claims 3-4, 16, 28, and 32, and the associated dependent claims 5-8, 17-24, and 29-30, are not obvious variants of claims 4-5, 7-8, and 14 of the '341 patent.

Applicants' claims 10, 12-13, 21, and 23-24 recite an implant having a compressive strength of at least about 120 MPa. These claims are patentably distinct from the paste or putty recited in claims 4-5, 7-8, and 14 of the '341 patent, which would not be expected to provide this very high degree of compressive strength.

Applicants' claims 25-32 recite methods of bone implantation and spinal fusion. In contrast, claims 4-5, 7-8, and 14 of the '341 patent are directed to implant materials and methods of preparing an implant. Furthermore, Applicants' claims 26 and 29 recite that conversion of the implanted calcium phosphate material to poorly-crystalline hydroxyapatite is completed in a time between about 2 weeks and about 6 weeks after implantation. Nothing in claims 4-5, 7-8, and 14 of the '341 patent suggests such a slowly converting material, and claim 19, which recites an *in vivo* hardening time of 60 minutes or less, suggests that the materials claimed in the '341 patent harden to form poorly crystalline apatitic calcium phosphate much more quickly. Thus, the methods of bone implantation and spinal fusion recited in Applicants' claims 25-32 are patentably distinct from claims 4-5, 7-8, and 14 of the '341 patent.

Furthermore, with respect to pending claims 9, 10, 20, and 21, the combination of claims 4-5, 7-8, and 14 of the '341 patent with the disclosure of the '456 patent would also fail to support a rejection of pending claims 9, 10, 20, and 21 for obviousness-type double patenting. As is discussed above, neither the claims of the '341 patent, nor the disclosure of the '456 patent discloses a composition with the compressive strength characteristics recited in the pending claims. Both the claims of the '341 patent and the specification of the '456 patent fail to teach or suggest a composition with a compressive strength of 60 MPa, as is recited in present claims 1 and 16, from which claims 9 and 20 depend, much less a compressive strength of 120 MPa, as is recited in present claims 10 and 21. The '456 patent also fails to provide a reasonable expectation of success in producing a composition with the compressive strength characteristics recited in the pending claims (discussed *supra*). For these reasons as well, pending claims 9, 10,

20, and 21 are patentably distinct over claims 4-5, 7-8, and 14 of the '341 patent in view of the '456 patent.

The above arguments make clear that none of the pending claims 1-13 and 16-32 is an obvious variant of any of the cited claims of the '341 patent, when examined alone or in combination with the '456 patent. The same arguments would apply with respect to new dependent claims 33-36, which depend from rejected claims 1, 16, 25, and 28, respectively, to the extent that the Examiner would apply the double patenting rejection to the new claims. The double patenting rejection is moot with respect to claims 14-15, which have been canceled. Thus, Applicants respectfully request that the present obviousness-type double patenting rejection be reconsidered and withdrawn.

CONCLUSION

In view of the above remarks, Applicants respectfully submit that the claims are in condition for allowance, and such action is respectfully requested.

Enclosed is a petition to extend the period for replying for three months, to and including November 2, 2003, and a check for the fee required under 37 C.F.R. § 1.17(a).

Also enclosed is a check for $18.00 for the addition of two more claims in excess of twenty (four claims have been added, while two were canceled). No other fees are believed to be due in connection with this correspondence.

Applicants note that the Office action was mailed to the incorrect address. Effective immediately, please address all communication in this application to:

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If there are any additional charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

Date: Nov. 3, 2003

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